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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,752	IKEDA, KEIKO	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-9* is/are pending in the application.

4a) Of the above claim(s) *5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1 and 3-9 are pending in the application.

[2] Applicant's amendment to the claims, filed on 3/14/08, is acknowledged. Claims 1 and 3-9 have been amended and claim 2 has been canceled. This listing of the claims replaces all prior versions and listings of the claims.

[3] Receipt of a Declaration by Keiko Ikeda under 37 CFR 1.132, filed on 3/14/08, is acknowledged.

[4] Applicant's arguments filed on 3/14/08 in response to the non-final Office action filed on 12/20/07 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity

[6] Applicant continues to traverse the restriction requirement on the grounds that: 1) the protein complex of claim 1 is not taught by Ikeda et al. and 2) claim 9 has been amended to "become directed to" an isolated protein complex.

With respect to argument 2), applicant's argument is found persuasive and claim 9 has been co-examined with elected claims 1, 3-4, and 6-8. However, applicant's argument 1) is not found persuasive. According to PCT Rule 13.2 unity of invention

exists only when the shared same or corresponding special technical feature is a contribution over the prior art. The inventions of Group I (claims 1, 3-4, and 6-9) and Group II (claim 5) do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. The technical feature of Group I is a protein complex and the technical feature of Group II is a method for producing a protein complex, which are shown by Ohta et al. (WO 02/36785; cited as reference AF in the IDS filed on 7/8/05) to lack novelty or inventive step because the reference teaches a protein complex encompassed by claim 1 and a method of making said protein complex (see particularly the noted teachings of Ohta at p. 17 of the Office action filed on 12/20/07), and thus the shared same or coresponding special technical feature of Groups I-II is not a contribution over the prior art.

[7] Claim 5 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/9/07.

[8] Claims 1, 3-4, and 6-9 are being examined on the merits.

Priority

[9] As noted in the prior Office action, applicant's claim to foreign priority under 35 USC § 119(a)-(d) to Japanese application JP 2003-005099, filed on 1/10/03, is acknowledged. A certified copy of the foreign priority document has been filed in the

instant application on 7/8/05. The priority claim is set forth in the Declaration filed under 37 CFR 1.63 on 2/7/06.

Specification/Informalities

[10] The objection to the specification as having a title that is not descriptive is with withdrawn in view of the instant amendment to the specification.

Claim Objection

[11] The objection to claim 2 under CFR 1.75(c) for failing to further limit the subject matter of a previous claim is withdrawn in view of the cancellation of the claim.

Claim Rejections - 35 USC § 101

[12] The rejection of claims 1-4 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of cancellation of claim 2 and amendment to claims 1 and 3-4 to insert the term "isolated".

Claim Rejections - 35 USC § 112, Second Paragraph

[13] The rejection of claim 2 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the cancellation of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

[14] The written description rejection of claims 1, 3-4, and 6-8 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 10 beginning at p. 7 of the Office action filed on 12/20/07. In view of the instant claim amendment , claim 9 has been included in the rejection. Thus, claims 1, 3-4, and 6-9 are rejected herein.

RESPONSE TO ARGUMENT: Applicant argues the rejection is obviated by amendment to recite the amino acid residues of the "restricted region", namely the limitation "wherein the restricted region of capsid protein VP3 is a region from the 41st amino acid residue to the 79th amino acid residue".

Applicant's argument is not found persuasive. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial

variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only the single representative species of the claimed or recited genus of protein complexes, i.e., a protein complex of a target protein fused to the C-terminus of BmCPV strain H VP3 protein amino acids 41-79 occluded within the BmCPV strain H polyhedrin. Other than this single species, the specification fails to disclose other representative species of the genus of claimed protein complexes. In this case, the genus of protein complexes encompasses widely variant species, including a protein complex of any target protein having a "restricted region" of any VP3 protein of any CPV as an embedding signal for polyhedron. The disclosure of the single representative species of protein complexes as noted above fails to reflect the variation among the members of the genus. In this case, the genus of protein complexes is required to have the structural feature of a "restricted region" which functions "as an embedding signal for polyhedron". However, the specification characterizes only one such structure-function relationship, *i.e.,* the "restricted region" of BmCPV strain H VP3, which is defined in the specification as "either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue" (p. 6, second paragraph).

Although it is acknowledged that the claims are unlimited with respect to CPV that is the source of the VP3 protein, it is noted that even among *Bombyx mori* CPV, Hagiwara et al. (*J. Gen. Virol.* 83:1477-1482, 2002; cited as reference AO in the IDS filed on 7/8/05) discloses that *B. mori* CPVs "can be divided into nine strains…distinguished by the shapes and/or the intracellular localization of the inclusion

bodies" (p. 1477, column 2, top). Given that the specification discloses only a single representative species of the genus of VP3 polypeptides, *i.e.,* BmCPV strain H VP3, the corresponding BmCPV strain H polyhedrin, and the structure-function relationship between the "restricted region" of BmCPV strain H VP3 and its function of being an "embedding signal" for the BmCPV strain H polyhedrin, the species encompassed by the genus are widely variant and given the lack of description of a representative number of compounds sufficient to reflect that variation, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[15] The scope of enablement rejection of claims 1, 3-4, and 6-8 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 11 beginning at p. 10 of the Office action filed on 12/20/07. In view of the instant claim amendment , claim 9 has been included in the rejection. Thus, claims 1, 3-4, and 6-9 are rejected herein.

RESPONSE TO ARGUMENT: Applicant argues the rejection is obviated by amendment to recite the amino acid residues of the "restricted region", namely the limitation "wherein the restricted region of capsid protein VP3 is a region from the 41st amino acid residue to the 79th amino acid residue".

Applicant's argument is not found persuasive. The Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: According to MPEP 2164.04, "[b]efore any analysis of enablement can occur, it is necessary for the examiner to construe the claims…and explicitly set forth the scope of the claim when writing an Office action." MPEP 2164.08 states, "[a]ll questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner determine exactly what subject matter is encompassed by the claims…claims are to be given their broadest reasonable interpretation that is consistent with the specification."

The claims are so broad as to encompass any protein complex comprising a polyhedral protein having an insect virus encapsulated therein and a target protein having a restricted region of a capsid protein VP3 (amino acids 41 to 79) of cytoplasmic polyhedrosis virus as an embedding signal for polyhedron and a biosensor comprising said protein complex. The source of the polyhedrin is unlimited, while the source of the recited VP3 protein is limited to being a CPV VP3 polypeptide, albeit the structure, *i.e.,* amino acid sequence of the VP3, is unlimited. Also, in view of the disclosure of the specification, it appears that applicant intends for "VP3" to encompass not only full-length proteins, but to also encompass fragments of CPV VP3 polypeptides. The broad scope of the claims is not commensurate with the enablement provided by the disclosure, particularly with regard to the CPV VP3 polypeptide and corresponding polyhedron, where the CPV VP3 polypeptide has a "restricted region...as an embedding

signal for polyhedron". According to the specification, the “restricted region” is defined as “either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue” (p. 6, second paragraph).

The state of the prior art; The level of one of ordinary skill; The level of predictability in the art: Protein complexes of a target protein occluded by the polyhedra of *nuclear* polyhedrosis viruses are well-known in the prior art. However, application of this concept to other viruses, *e.g.,* CPVs, appears to require knowledge of those regions of the polyhedra that are non-essential for crystallization and interactions between the proteins of the polyhedron and proteins occluded thereby. In this case, Ikeda et al. (*supra*) and Ohta et al. (WO 02/36785; cited in the IDS filed on 7/8/05 as reference AF) disclose the sequence of the BmCPV H strain VP3 polypeptide. However, the prior art does not appear to characterize this interaction in any other CPVs as broadly encompassed by the claims. As noted in Ikeda et al. (*supra*), “little is known about the specific interactions between CPV polyhedron and the viral capsid protein,” particularly the interaction between CPV polyhedron and VP3 (p. 994, column 1, middle). Thus, other than the interaction between BmCPV strain H polyhedrin and VP3, there is no way to predict interaction of any VP3 protein of any strain of *Bombyx mori* CPV with any other strain of *B. mori* CPV polyhedrin to achieve a protein complex as encompassed by the claims. Furthermore, it is noted that the post-filing reference of Mori et al. (*J. Biol. Chem.* 282:1728917296, 2007; “Mori”), in disclosing production of *B. mori* CPV polyhedra containing human FGF-2, teaches that “only degradation products of FGF-2

were found in polyhedra where FGF-2 was fused with VP3 at the N terminus" (p. 17292, column 1, first paragraph). Moreover, as evidenced by the instant specification, C-terminal deletions of VP3 disrupt immobilization of a target protein into polyhedra (Figure 3).

The amount of direction provided by the inventor; The existence of working examples: The specification's working examples of the claimed protein complex is a protein complex of a target protein fused to the C-terminus of at least BmCPV strain H VP3 amino acids 1-79 embedded within the BmCPV strain H polyhedrin. Other than this working example, the specification fails to provide the necessary specific guidance for isolating other BmCPV VP3 polypeptides. Further, the specification fails to provide guidance for interchanging the VP3 protein from one strain of CPV with the polyhedrin of any other virus with an expectation of achieving a protein complex as encompassed by the claims.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the state of the art regarding interaction between viral polyhedrin and CPV VP3 proteins, and the high level of unpredictability as noted above, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation

with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections – Double Patenting

[16] The provisional obviousness-type double patenting rejection of claims 1, 3-4, and 6-8 under the judicially created doctrine of obviousness-type double patenting is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 12 beginning at p. 14 of the Office action filed on 12/20/07. Amended claim 9 is included in the instant provisional rejection. Thus, claims 1, 3-4, and 6-9 are provisionally rejected. In order to clarify the record, it is noted that the provisional rejection as set forth in the 12/20/07 Office action states claims 7-8 as being unpatentable over claims 1-8 and 18 of co-pending application No. 10/415,096 in view of Hosokawa et al. and Ito et al. However, this is an inadvertent oversight on the part of the examiner. The examiner intended to state that claim 6 – not claims 7and 8 – was unpatentable over claims of the '096 application in view of Hosokawa et al. and Ito et al. That the examiner intended to state that claim 6 – not claims 7and 8 – is unpatentable over claims of the '096 application in view of Hosokawa et al. and Ito et al. is clear from reviewing the rejections under 35 U.S.C. 103(a).

RESPONSE TO ARGUMENT: Applicant argues the provisional rejection is obviated since the claimed invention is patentably distinguished over Ohta for reasons noted below in response to the rejection under 35 U.S.C. 102/103. However, this is not found persuasive because applicant's claimed invention fails to distinguish over the Ohta reference for reasons of record and reasons set forth below.

Claim Rejections - 35 USC § 102/103

[17] The rejection of claims 1 and 3-4 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ohta et al. (WO 02/36785; cited in the IDS filed on 7/8/05 as reference AF; "Ohta") is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 13 beginning at p. 16 of the Office action filed on 12/20/07.

RESPONSE TO ARGUMENT: Applicant argues: 1) Ohta fails to identify that portion of *B. mori* H strain CPV VP3 that is the polyhedron embedding signal and 2) without using only the recited fragment of VP3 limited to the embedding signal, proper activity of the target protein will not be obtained.

Applicant's argument is not found persuasive. Here, it appears that applicant intends for the "restricted region" of the target protein of claim 1 to be limited to residues 41-79 of a VP3 protein. However, it is noted that claim 1 recites "a target protein *having* a restricted region…", where the term "having" has been broadly, but reasonably interpreted as open-ended and being synonymous with "comprising". While it is

acknowledged that Ohta fails to expressly teach or suggest that the embedding signal of *B. mori* strain H CPV VP3 is residues 41-79, the protein of Ohta nonetheless has this embedding signal, which is undisputed by applicant. According to MPEP 2112.I, "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999)" and MPEP 2112.II states, "There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of invention*, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003)". As such, even thought Ohta fails expressly teach or suggest that the embedding signal of *B. mori* H strain CPV VP3 is residues 41-79, the Ohta reference nonetheless anticipates the claimed invention.

[18] The rejection of claims 1, 3-4, and 6-8 under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Mori et al. (JP 2003-155300, 2003; "Mori") is withdrawn in view of the instantly filed Declaration by Keiko Ikeda under 37 CFR 1.132.

Claim Rejections - 35 USC § 103

[19] The rejection of claim 6 under 35 U.S.C. 103(a) as being unpatentable over Ohta (*supra*) in view of Hosokawa et al. (Materials Research Society, Symposium C, Bio-

Inspired Nanoscale Hybrid Systems, December 2002, Abstract C3.5; available at www.mrs.org/s_mrs/bin.asp?CID=2109&DID=91203&DOC=FILE.PDF; "Hosokawa") and Ito et al. (*Appl. Physics Lett.* 78:2566-2568, 2001; "Ito") is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 15 beginning at p. 19 of the Office action filed on 12/20/07.

RESPONSE TO ARGUMENT: Applicant argues the references of Hosokawa and Ito fail to remedy the alleged deficiencies of Ohta. However, this is not found persuasive because the features upon which applicant relies to distinguish the claimed invention over Ohta are not present in claim 6. Even assuming *arguendo* the limitations were present, applicant's alleged deficiencies of Ohta are improperly based upon: 1) only the *express* teachings of Ohta without considering the implicit and inherent teachings and 2) limitations that are not recited in the claims. The examiner maintains the position that the combination of references is sufficient to establish a *prima facie* case of obviousness.

[20] The rejection of claims 7-8 under 35 U.S.C. 103(a) as being unpatentable over Ohta (*supra*) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 16 beginning at p. 22 of the Office action filed on 12/20/07. Amended claim 9 is included in the instant rejection since Ohta contemplates an enzyme being encompassed by the BmCPV virion (see, *e.g.,* p. 1, paragraph 14 of US Patent Application Publication

2004/59091, which is relied upon as an English-language translation of Ohta). Thus, claims 7-9 are rejected.

RESPONSE TO ARGUMENT: Applicant argues the claimed invention is distinguished over Ohta for reasons noted above in response to the rejection under 35 U.S.C. 102/103. However, this is not found persuasive because the features upon which applicant relies to distinguish the claimed invention over Ohta are not present in claims 7-9. Even assuming *arguendo* the limitations were present, applicant's alleged deficiencies of Ohta are improperly based upon: 1) only the *express* teachings of Ohta without considering the implicit and inherent teachings and 2) limitations that are not recited in the claims. The examiner maintains the position that Ohta is sufficient to establish a *prima facie* case of obviousness.

Conclusion

[21] Status of the claims:

- Claims 1 and 3-9 are pending.
- Claim 5 is withdrawn from consideration.
- Claims 1, 3-4, and 6-9 are rejected.
- No claim is in condition for allowance.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Steadman/
David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656